

**Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings of claims in the application:

**Listing of Claims:**

380. (Currently Amended) A method for conjugating a peptide immunogen comprising A $\beta$  peptide or fragments of A $\beta$  or analogs thereof via a reactive group of an amino acid residue of the peptide immunogen to a protein/polypeptide carrier having one or more functional groups, the method comprising the steps of:

(a) derivatizing one or more of the functional groups of the protein/polypeptide carrier or optionally to a polypeptide linker attached to the protein/polypeptide carrier to generate a derivatized carrier with reactive sites;

(b) reacting the derivatized protein/polypeptide carrier of step (a) with a reactive group of an amino acid of the peptide immunogen comprising A $\beta$  peptide or fragments of A $\beta$  or analogs thereof under reaction conditions such that the peptide immunogen is conjugated to the derivatized protein/polypeptide carrier via at least one of the reactive sites, thereby forming a conjugate; and

(c) further reacting the conjugate with a capping reagent to ~~inactivate~~inactive free, reactive unreacted reactive sites on the derivatized protein/polypeptide carrier, whereby the conjugate elicits a desired immune against the A $\beta$  peptide.

381. (Previously Presented) The method of claim 380, wherein the protein/polypeptide carrier is selected from the group consisting of human serum albumin, keyhole limpet hemocyanin (KLH), immunoglobulin molecules, thyroglobulin, ovalbumin, influenza hemagglutinin, PADRE polypeptide, malaria circumsporozoite (CS) protein, hepatitis B surface antigen (HBsAg19-28), Heat Shock Protein (HSP) 65, *Mycobacterium tuberculosis*, cholera toxin, cholera toxin mutants with reduced toxicity, diphtheria toxin, CRM<sub>197</sub> protein that is cross-reactive with diphtheria toxin, recombinant Streptococcal C5a peptidase, *Streptococcus pyogenes* ORF1224, *Streptococcus pyogenes* ORF1664, *Streptococcus pyogenes* ORF2452, *Streptococcus pneumoniae* pneumolysin, pneumolysin mutants with reduced toxicity, *Chlamydia*

*pneumoniae* ORF T367, *Chlamydia pneumoniae* ORF T858, Tetanus toxoid, HIV gp120 T1, components recognizing microbial surface adhesive matrix molecules (MSCRAMMS), growth factors, hormones, cytokines and chemokines.

382. (Previously Presented) The method of claim 381, wherein the protein/polypeptide carrier is CRM<sub>197</sub>.

383. (Previously Presented) The method of claim 380, wherein the peptide immunogen is an A $\beta$  fragment.

384. (Previously Presented) The method of claim 383, wherein the A $\beta$  fragment is selected from the group consisting of A $\beta$ 1-3, 1-4, 1-5, 1-6, 1-7, 1-9, 1-10, 1-11, 1-12, 1-16, 1-28, 3-6, 3-7, 13-28, 15-24, 16-22, 16-23, 17-23, 17-24, 18-24, 18-25, 17-28, 25-35, 33-42, 35-40, and 35-42.

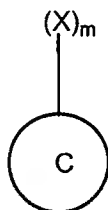
385. (Previously Presented) The method of claim 384, wherein the A $\beta$  fragment is A $\beta$ 1-7.

386. (Previously Presented) The method of claim 380, wherein the functional group of one or more amino acid molecules of the protein/polypeptide carrier or of the optionally attached polypeptide linker is derivatized using a cross-linking reagent.

387. (Previously Presented) The method of claim 386, wherein the protein/polypeptide carrier is reacted with a haloacetylating agent.

388. (Previously Presented) The method of claim 380, wherein the capping reagent that is used to inactivate free reactive, functional group on the activated protein/polypeptide carrier is selected from the reagent group consisting of cysteamine, N-acetylcysteamine, ethanolamine, sodium hydroxide, sodium carbonate, ammonium bicarbonate and ammonia.

389. (Previously Presented) A method for conjugating a peptide immunogen comprising A $\beta$  peptide or fragments of A $\beta$  or analogs thereof to a protein/polypeptide carrier having the structure:



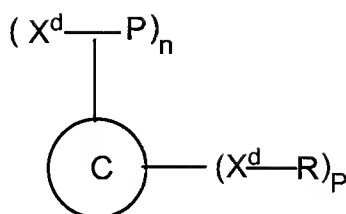
wherein,

C is a protein/polypeptide carrier and X is a derivatizable functional group of an amino acid residue on the protein/polypeptide carrier or optionally of an amino acid residue of a peptide linker covalently attached to the protein/polypeptide carrier, and wherein m is an integer greater than 0, but less than or equal to 85, the method comprising the steps of:

(a) derivatizing one or more of the functional groups of the protein/polypeptide carrier or of the optionally attached linker molecule to generate a derivatized molecule with reactive sites;

(b) reacting the derivatized protein/polypeptide carrier of step (a) with a reactive group of an amino acid of the peptide immunogen comprising A $\beta$  peptide or fragments of A $\beta$  or analogs thereof to form a covalently coupled peptide immunogen-protein/polypeptide carrier conjugate; and

(c) further reacting the said conjugate with a capping reagent to inactivate the free reactive functional groups on the activated protein/polypeptide carrier, such that the capped groups are not free to react with other molecules, thereby preserving the functionality of the carrier, such that it retains its ability to elicit the desired immune responses against the peptide immunogen that would otherwise not occur without a carrier, so as to generate a capped peptide immunogen-protein/polypeptide carrier conjugate having the formula:



wherein,

C is the protein/polypeptide carrier and  $X^d$  is a derivatized functional group of an amino acid residue of the protein/polypeptide carrier or optionally of an amino acid residue of a peptide linker covalently attached to the protein/polypeptide carrier, and, wherein,

P is a peptide immunogen comprising A $\beta$  peptide or fragments of A $\beta$  or analogs thereof covalently attached to the derivatized functional group of the amino acid residue of the protein carrier or optionally of an amino acid residue of a peptide linker covalently attached to a protein/polypeptide carrier,

R is a capping molecule covalently attached to the derivatized functional group of an amino acid residue of the protein/polypeptide carrier or optionally of an amino acid residue of a peptide linker covalently attached to a protein/polypeptide carrier,

n is an integer greater than 0, but less than or equal to 85, and

p is an integer greater than 0, but less than 85.

390. (Previously Presented) The method of claim 389, wherein the protein/polypeptide carrier is selected from the group consisting of human serum albumin, keyhole limpet hemocyanin (KLH), immunoglobulin molecules, thyroglobulin, ovalbumin, influenza hemagglutinin, PADRE polypeptide, malaria circumsporozoite (CS) protein, hepatitis B surface antigen (HBsAg19-28), Heat Shock Protein (HSP) 65, *Mycobacterium tuberculosis*, cholera toxin, cholera toxin mutants with reduced toxicity, diphtheria toxin, CRM<sub>197</sub> protein that is cross-reactive with diphtheria toxin, recombinant Streptococcal C5a peptidase, *Streptococcus pyogenes* ORF1224, *Streptococcus pyogenes* ORF1664, *Streptococcus pyogenes* ORF2452, *Streptococcus pneumoniae* pneumolysin, pneumolysin mutants with reduced toxicity, *Chlamydia pneumoniae* ORF T367, *Chlamydia pneumoniae* ORF T858, Tetanus toxoid, HIV gp120 T1,

components recognizing microbial surface adhesive matrix molecules (MSCRAMMS), growth factors, hormones, cytokines and chemokines.

391. (Previously Presented) The method of claim 390, wherein the protein/polypeptide carrier is CRM<sub>197</sub>.

392. (Previously Presented) The method of claim 389, wherein the peptide immunogen is an A $\beta$  fragment.

393. (Previously Presented) The method of claim 392, wherein the A $\beta$  fragment is selected from the group consisting of A $\beta$ 1-3, 1-4, 1-5, 1-6, 1-7, 1-9, 1-10, 1-11, 1-12, 1-16, 1-28, 3-6, 3-7, 13-28, 15-24, 16-22, 16-23, 17-23, 17-24, 18-24, 18-25, 17-28, 25-35, 33-42, 35-40, and 35-42.

394. (Previously Presented) The method of claim 393, wherein the A $\beta$  fragment is A $\beta$ 1-7.

395. (Previously Presented) The method of claim 389, wherein the functional group of one or more amino acid molecules of the protein/polypeptide carrier or of the optionally attached polypeptide linker is derivatized using a cross-linking reagent.

396. (Previously Presented) The method of claim 395, wherein the protein/polypeptide carrier is reacted with a haloacetylating agent.

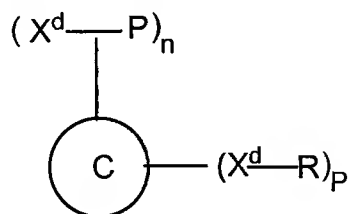
397. (Previously Presented) The method of claim 389, wherein the capping reagent that is used to inactivate free reactive, functional group on the activated protein/polypeptide carrier is selected from the reagent group consisting of cysteamine, N-acetylcysteamine, ethanolamine, sodium hydroxide, sodium carbonate, ammonium bicarbonate and ammonia.

398. (Previously Presented) A conjugate comprising a peptide immunogen-protein/polypeptide carrier conjugate wherein the protein/polypeptide carrier has the formula:



wherein,

C is a protein/polypeptide carrier and X is a derivatizable functional group of an amino acid residue on the protein/polypeptide carrier or optionally of an amino acid residue of a peptide linker covalently attached to the protein/polypeptide carrier, and, wherein m is an integer greater than 0, but less than or equal to 85, and wherein the peptide immunogen-protein/polypeptide carrier conjugate has the formula:



wherein,

C is the protein/polypeptide carrier and  $X^d$  is a derivatized functional group of an amino acid residue of the protein/polypeptide carrier or optionally of an amino acid residue of a peptide linker covalently attached to the protein/polypeptide carrier, and, wherein, P is a peptide immunogen comprising A $\beta$  peptide or fragments of A $\beta$  or analogs thereof covalently attached to the derivatized functional group of the amino acid residue of the protein carrier or optionally of an amino acid residue of a peptide linker covalently attached to a protein/polypeptide carrier, R is a capping molecule covalently attached to the derivatized functional group of an amino acid residue of the protein/polypeptide carrier or optionally of an amino acid residue of a peptide linker covalently attached to a protein/polypeptide carrier, thereby preserving the functionality of the carrier such that it retains its ability to elicit the desired immune responses against the peptide immunogen comprising the A $\beta$  peptide or fragments of A $\beta$  or analogs thereof that would otherwise not occur without a carrier, n is an integer greater than 0, but less than or equal to 85, and p is an integer greater than 0, but less than 85.

399. (Currently Amended) The conjugate of claim 398, wherein the protein/polypeptide carrier is selected from the group consisting of human serum albumin, keyhole limpet hemocyanin (KLH), immunoglobulin molecules, thyroglobulin, ovalbumin, influenza hemagglutinin, PADRE polypeptide, malaria circumsporozoite (CS) protein, hepatitis B surface antigen (HBsAg19-28), Heat[[eat]] Shock Protein (HSP) 65, *Mycobacterium tuberculosis*, cholera toxin, cholera toxin mutants with reduced toxicity, diphtheria toxin, CRM<sub>197</sub> protein that is cross-reactive with diphtheria toxin, recombinant Streptococcal C5a peptidase, *Streptococcus pyogenes* ORF1224, *Streptococcus pyogenes* ORF1664, *Streptococcus pyogenes* ORF2452, *Streptococcus pneumoniae* pneumolysin, pneumolysin mutants with reduced toxicity, *Chlamydia pneumoniae* ORF T367, *Chlamydia pneumoniae* ORF T858, Tetanus toxoid, HIV gp120 T1, components recognizing microbial surface adhesive matrix molecules (MSCRAMMS), growth factors, hormones, cytokines and chemokines.

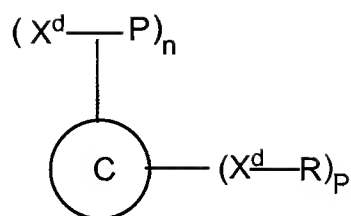
400. (Previously Presented) The conjugate of claim 399, wherein the protein/polypeptide carrier is CRM<sub>197</sub>.

401. (Previously Presented) The conjugate of claim 398 wherein the peptide immunogen is an A $\beta$  fragment.

402. (Previously Presented) The conjugate of claim 401, wherein the A $\beta$  fragment is selected from the group consisting of A $\beta$ 1-3, 1-4, 1-5, 1-6, 1-7, 1-9, 1-10, 1-11, 1-12, 1-16, 1-28, 3-6, 3-7, 13-28, 15-24, 16-22, 16-23, 17-23, 17-24, 18-24, 18-25, 17-28, 25-35, 33-42, 35-40, and 35-42.

403. (Previously Presented) The conjugate of claim 402, wherein the A $\beta$  fragment is A $\beta$ 1-7.

404. (Previously Presented) A peptide immunogen-protein/polypeptide carrier conjugate generated according to the method of claim 389 and having the formula:



wherein,

C is the protein/polypeptide carrier and  $X^d$  is a derivatized functional group of an amino acid residue of the protein/polypeptide carrier or optionally of an amino acid residue of a peptide linker covalently attached to the protein/polypeptide carrier, and, wherein, P is a peptide immunogen molecule comprising A $\beta$  peptide or fragments of A $\beta$  or analogs thereof covalently attached to the derivatized functional group of the amino acid residue of the protein carrier or optionally of an amino acid residue of a peptide linker covalently attached to a protein/polypeptide carrier, R is a capping molecule covalently attached to the derivatized functional group of an amino acid residue of the protein/polypeptide carrier or optionally of an amino acid residue of a peptide linker covalently attached to a protein/polypeptide carrier, which preserves the functionality of the carrier, such that it retains its ability to elicit the desired immune responses against the peptide immunogen that would otherwise not occur without a carrier, n is an integer greater than 0, but less than or equal to 85, and p is an integer greater than 0, but less than 85.

405. (Previously Presented) The conjugate of claim 404, wherein the protein/polypeptide carrier is selected from the group consisting of human serum albumin, keyhole limpet hemocyanin (KLH), immunoglobulin molecules, thyroglobulin, ovalbumin, influenza hemagglutinin, PADRE polypeptide, malaria circumsporozite (CS) protein, hepatitis B surface antigen (HBsAg19-28), Heat Shock Protein (HSP) 65, *Mycobacterium tuberculosis*, cholera toxin, cholera toxin mutants with reduced toxicity, diphtheria toxin, CRM<sub>197</sub> protein that is cross-reactive with diphtheria toxin, recombinant Streptococcal C5a peptidase, *Streptococcus pyogenes* ORF1224, *Streptococcus pyogenes* ORF1664, *Streptococcus pyogenes* ORF2452, *Streptococcus pneumoniae* pneumolysin, pneumolysin mutants with reduced toxicity, *Chlamydia pneumoniae* ORF T367, *Chlamydia pneumoniae* ORF T858, Tetanus toxoid, HIV gp120 T1,



components recognizing microbial surface adhesive matrix molecules (MSCRAMMS), growth factors, hormones, cytokines and chemokines.

406. (Previously Presented) The conjugate of claim 405, wherein the protein/polypeptide carrier is CRM<sub>197</sub>.

407. (Previously Presented) The conjugate of claim 404 wherein the peptide immunogen is an A $\beta$  fragment.

408. (Previously Presented) The conjugate of claim 407, wherein the A $\beta$  fragment is selected from the group consisting of A $\beta$ 1-3, 1-4, 1-5, 1-6, 1-7, 1-9, 1-10, 1-11, 1-12, 1-16, 1-28, 3-6, 3-7, 13-28, 15-24, 16-22, 16-23, 17-23, 17-24, 18-24, 18-25, 17-28, 25-35, 33-42, 35-40, and 35-42.

409. (Previously Presented) The conjugate of claim 408, wherein the A $\beta$  fragment is A $\beta$ 1-7.

410. (Previously Presented) An immunogenic composition, comprising a conjugate of a peptide immunogen with a protein/polypeptide carrier generated by the method of claim 389, together with one or more pharmaceutically acceptable excipients, diluents, and /or adjuvants.

411. (Previously Presented) The immunogenic composition of claim 410, wherein the protein/polypeptide carrier is selected from the group consisting of human serum albumin, keyhole limpet hemocyanin (KLH), immunoglobulin molecules, thyroglobulin, ovalbumin, influenza hemagglutinin, PADRE polypeptide, malaria circumsporozoite (CS) protein, hepatitis B surface antigen (HBsAg19-28), Heat Shock Protein (HSP) 65, *Mycobacterium tuberculosis*, cholera toxin, cholera toxin mutants with reduced toxicity, diphtheria toxin, CRM<sub>197</sub> protein that is cross-reactive with diphtheria toxin, recombinant Streptococcal C5a peptidase, *Streptococcus pyogenes* ORF1224, *Streptococcus pyogenes* ORF1664, *Streptococcus pyogenes* ORF2452, *Streptococcus pneumoniae* pneumolysin, pneumolysin mutants with

reduced toxicity, *Chlamydia pneumoniae* ORF T367, *Chlamydia pneumoniae* ORF T858, Tetanus toxoid, HIV gp120 T1, components recognizing microbial surface adhesive matrix molecules (MSCRAMMS), growth factors, hormones, cytokines and chemokines.

412. (Previously Presented) The immunogenic composition of claim 411, wherein the protein/polypeptide carrier is CRM<sub>197</sub>.

413. (Previously Presented) The immunogenic composition of claim 410 wherein the peptide immunogen is an A $\beta$  fragment.

414. (Previously Presented) The immunogenic composition of claim 413, wherein the A $\beta$  fragment is selected from the group consisting of A $\beta$ 1-3, 1-4, 1-5, 1-6, 1-7, 1-9, 1-10, 1-11, 1-12, 1-16, 1-28, 3-6, 3-7, 13-28, 15-24, 16-22, 16-23, 17-23, 17-24, 18-24, 18-25, 17-28, 25-35, 33-42, 35-40, and 35-42.

415. (Previously Presented) The immunogenic composition of claim 414, wherein the A $\beta$  fragment is A $\beta$ 1-7.

416. (Previously Presented) The immunogenic composition of claim 410, wherein one or more adjuvants are selected from the group consisting of GM-CSF, 529 SE, IL-12, aluminum phosphate, aluminum hydroxide, *Mycobacterium tuberculosis*, *Bordetella pertussis*, bacterial lipopolysaccharides, aminoalkyl glucosamine phosphate compounds, MPL<sup>TM</sup> (3-O-deacylated monophosphoryl lipid A), a polypeptide, Quil A, STIMULON<sup>TM</sup> QS-21, a pertussis toxin (PT), an E. coli heat-labile toxin (LT), IL-1  $\alpha$ , IL-1  $\beta$ , IL-2, IL-4, IL-5, IL-6, IL-7, IL-8, IL-10, IL-13, IL-14, IL-15, IL-16, IL-17, IL-18, interferon-  $\alpha$ , interferon-  $\beta$ , interferon- $\gamma$ , G-CSF, TNF-  $\alpha$  and TNF- $\beta$ .

417. (Previously Presented) A method for inducing an immune response in a mammalian subject, which comprises administering an effective amount of the immunogenic composition of claim 410 to the subject.

418. (Previously Presented) The method of claim 417, wherein the protein/polypeptide carrier is selected from the group consisting of human serum albumin, keyhole limpet hemocyanin (KLH), immunoglobulin molecules, thyroglobulin, ovalbumin, influenza hemagglutinin, PADRE polypeptide, malaria circumsporozoite (CS) protein, hepatitis B surface antigen (HBsAg19-28), Heat Shock Protein (HSP) 65, *Mycobacterium tuberculosis*, cholera toxin, cholera toxin mutants with reduced toxicity, diphtheria toxin, CRM<sub>197</sub> protein that is cross-reactive with diphtheria toxin, recombinant Streptococcal C5a peptidase, *Streptococcus pyogenes* ORF1224, *Streptococcus pyogenes* ORF1664, *Streptococcus pyogenes* ORF2452, *Streptococcus pneumoniae* pneumolysin, pneumolysin mutants with reduced toxicity, *Chlamydia pneumoniae* ORF T367, *Chlamydia pneumoniae* ORF T858, Tetanus toxoid, HIV gp120 T1, components recognizing microbial surface adhesive matrix molecules (MSCRAMMS), growth factors, hormones, cytokines and chemokines.

419. (Previously Presented) The method of claim 418, wherein the protein/polypeptide carrier is CRM<sub>197</sub>.

420. (Previously Presented) The method of claim 417, wherein the peptide immunogen is an A $\beta$  fragment.

421. (Previously Presented) The method of claim 420, wherein the A $\beta$  fragment is selected from the group consisting of A $\beta$ 1-3, 1-4, 1-5, 1-6, 1-7, 1-9, 1-10, 1-11, 1-12, 1-16, 1-28, 3-6, 3-7, 13-28, 15-24, 16-22, 16-23, 17-23, 17-24, 18-24, 18-25, 17-28, 25-35, 33-42, 35-40, and 35-42.

422. (Previously Presented) The method of claim 421, wherein the A $\beta$  fragment is A $\beta$ 1-7.

423. (Previously Presented) The method of claim 417, further comprising administering one or more adjuvants selected from the group consisting of GM-CSF, 529 SE, IL-12, aluminum phosphate, aluminum hydroxide, *Mycobacterium tuberculosis*, *Bordetella pertussis*, bacterial lipopolysaccharides, aminoalkyl glucosamine phosphate compounds, MPL™

(3-O-deacylated monophosphoryl lipid A), a polypeptide, Quil A, STIMULON™ QS-21, a pertussis toxin (PT), an E. coli heat-labile toxin (LT), IL-1  $\alpha$ , IL-1  $\beta$ , IL-2, IL-4, IL-5, IL-6, IL-7, IL-8, IL-10, IL-13, IL-14, IL-15, IL-16, IL-17, IL-18, interferon-  $\alpha$ , interferon-  $\beta$ , interferon- $\gamma$ , G-CSF, TNF-  $\alpha$  and TNF- $\beta$ .